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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,072	02/27/2002	Laurie DeLeve	13761-7065	1401

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,072	DELEVE, LAURIE	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/02/2004, 12/20/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 02, 2004 and December 20, 2004 has been entered. Pursuant to the grant of the Petition to revive issued on December 29, 2004, Examination on the merits of the pending claims continues.

Claims 1-19 are pending. New grounds of rejections are applied in view of newly discovered prior art.

Claim Objections

Claims 18 -20 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The claim 18 and 19 are directed to methods of treating a condition in a patient wherein the patient is suffering from the condition. Said claims appear to be duplicates of their base claims because in order to treat the claimed condition a patient must be suffering from that condition.

Claim 20 appears to be a duplicate of claim 11.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9, 11-12, 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Leitersdorf et al, Clinical Nephrology 1997, 48/1 (48-51) (abstract).

The instant claims are directed to methods of prophylaxis or treating Sinusoidal Obstruction Syndrome in a human patient in need thereof comprising administering an effective amount of a matrix metalloproteinase inhibitor.

Leitersdorf teaches administration of tetracyclines such as doxycycline in amount of about 100-600 mg/day to patients who have undergone liver transplantation and have developed nocardiosis. Such patients are viewed to fall within the scope of the instantly claimed patients in need because they are status post-liver transplantation and are subject immunosuppressive therapies that fall within the scope of the instantly claimed chemotherapy.

Note that in claims drawn to a process, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). Since Leitersdorf method meets the administration step and the patient population of the instant claims, it would inherently achieve the purpose of the instantly claimed invention by prophylactically treating, in human patients in need thereof,

sinusoidal obstruction syndrome or prophylactically treating chemotherapy induced liver disease including sinusoidal obstruction syndrome.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 13 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leitersdorf et al, Clinical Nephrology 1997, 48/1 (48-51) (abstract).

The teachings of Leitersdorf are described above. Leithersdorf only fails to explicitly teach a twice a day frequency for this method.

Nevertheless, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention would have been motivated to optimize the dosing frequency of Leitersdorf by routine experimentations.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of doxycycline or propionic acid derivatives for treating sinusoidal obstruction syndrome, it does not reasonably provide enablement for methods of treating such condition with all compounds that can potentially inhibit matrix metalloproteinases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to ascertain the entire scope of the term "matrix metalloproteinase inhibitor" and thus practice the invention commensurate in scope with these claims.

In particular, the specifications fail to enable the skilled artisan to practice the invention without undue experimentation. As held *in ex parte Forman* (230 USPQ 546, BdPatApp & Int.) and *In re Wands* (858 F.2d 731, 8 USPQ2d 1400, 1404, Fed. Cir.

1988) several factors are considered when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. In the instant case, the claims appear to be directed toward using such compounds that are not enabled by describing a function and thus reaching through a nonenabled invention. However, as set forth below, specification fails to enable one of ordinary skill in the art to practice the full scope of the claims.

Due to the unpredictable nature of the art, the level of one of ordinary skill in the art in assessing the entire scope of the term "matrix metalloproteinase inhibitor," the lack of working example and adequate guidance as to how to prepare all such compounds falling within the such language the specification fails to enable one of ordinary skill in the art to practice the claimed scope of the invention without undue experimentation.

(1) The nature of the invention:
The invention encompasses the entire genus of compounds that can inhibit the activity of metalloproteinase.

(2) The state of the prior art
The state of art towards accompolishing such activity is directed to various tetracycline derivatives and propionic acid derivatives. The art does not provide a common unifying structure or a structural activity relationship that can classify compounds as matrix metalloproteinase inhibitors.

(3) The relative skill of those in the art
The relative skill of those in the art is high and encompasses medicinal chemists and clinical pharmacologists.

(4) The predictability or unpredictability of the art
The unpredictability of the chemical art is very high as to determination of all compounds that can provide effective matrix metalloproeinase inhibition.

(5) The breadth of the claims

The claims are very broad. The instant claims are directed to the use of compounds that are identified by their ability to perform the function of inhibiting a matrix metalloproteinase. Accordingly, the claims appear to be directed to the use of a class of compounds that are identified by a function. The use of a functional limitation at the point of novelty is well explained by the Courts. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate." Also see *University of Rochester v. GD Searle & Co., Inc.* W.D.N.Y. 2003, (U.S. District Court for Western District United of New York).

Here, applicant's claims are directed to the use of a class of compounds that can be identified by a functional limitation. Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph, because it does not adequately "inform the public during the life of the patent of the limits of the monopoly asserted." *General Electric Company v. Wabash Appliance Corporation et* supra, at 468. Simply stated, the presented claims are an invitation to experiment, not reciting a specific compounds useful for practicing the instant invention.

(6) The amount of direction or guidance presented

The specification provides guidance to specific compounds known in the art to inhibit metalloproteinase. No commonality as to a common core or chemical characteristics have been described.

(7) The presence or absence of working examples

As stated above, the specification discloses specific set of compounds and not the entire genus of compounds encompassed by the term "matrix metalloproeinase inhibitor."

(8) The quantity of experimentation necessary

Since the ability of the compound to perform the described function is paramount to the scope of enablement of the claimed invention, the claims cannot be practiced of predicted by a prior knowledge. Rather, the scope of the claims must be determined on a case to case by painstaking experimental study. Accordingly, one of ordinary skill in the art would be burdened with undue experimentation study" to determine the all of the compounds capable of being used in the instant methods.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER